## REMARKS

### I. Status of Claims

Claims 1-48 are pending in this application. Applicants thank the Examiner for allowing claims 24-48 in this case.

### II. Rejections under 35 U.S.C. § 102(b)

#### A. Beasley et al.

The Office has maintained rejection of claims 1-4, 6-9, 11-15, and 17-20 under 35 U.S.C. § 102(b) as being anticipated by Beasley et al. (WO 97/04775) ("*Beasley*"). Office Action, pages 2 and 3. Specifically, the Office contends that *Beasley* discloses "8-ethyl-5,8-dihydro-5-oxo-2-(1-pyrrolidinyl)-pyrido[2,3-d]pyrimidine group," which falls within the definition of $R^5$ of the present invention, because $R^5$ is defined "to be [a] Hetar [group] which can be further condensed to a '5- to 7-membered heterocycle containing 1-3 heteroatoms chosen from N, O and S, which heterocycles can be substituted by oxo, etc'." *Id.* Therefore, the Office concludes that the compounds of formula (I) disclosed in *Beasley* contain the group corresponding to $R^5$ of the compounds claimed in the present invention. *Id.* Applicants respectfully disagree for at least the following reason.

First, Applicants respectfully submit that $R^5$ is not defined "to be [a] Hetar [group] which can be further condensed to a '5- to 7-membered heterocycle containing 1-3 heteroatoms chosen from N, O and S, which heterocycles can be substituted by oxo, etc'," as the Office contends. Instead, claim 1 of the present invention, for example, clearly defines that "$R^5$ is a group Hetar which can be unsubstituted or carry one or

more substituents chosen from . . . 5- to 7-membered heterocycles . . . wherein said heterocycles can optionally be condensed to said group Hetar." In other words, the present invention does not define that the Hetar group can be condensed to a 5- to 7-membered heterocycle. Instead, the 5- to 7-membered heterocycles can be chosen as the substituent for the $R^5$ group, and can optionally be condensed to the group Hetar (*i.e.*, the $R^5$ group as defined in, for example, claim 1). Therefore, in formula (I) of the present invention, the $R^5$ group, which is bonded to the C=O group of the NH-CO moiety, is a group Hetar as defined in, for example, claim 1, which can have at least one substituent chosen from 5- to 7-membered heterocycles and the 5- to 7-membered heterocycles (*i.e.*, the substiutent) can optionally be condensed to the group Hetar.

Furthermore, in the present invention, the group Hetar is defined as "a . . . aromatic . . . heterocycle." *E.g.*, claim 1. Therefore, the $R^5$ group of compounds of formula (I) in the present invention is an aromatic ring, which, as one of ordinary skill in the art know, should comprise a conjugated cyclic system of six pi electrons. In other words, the atom of the $R^5$ group, which is bonded directly to the C=O group of the NH-CO moiety in the formula (I) of the present invention should be an atom in an aromatic ring.

However, in the compounds of formula (I) of *Beasley*, the ring, which is bonded directly to the C=O group of the NH-CO moiety, such as 8-ethyl-5,8-dihydro-5-oxo-2-(1-pyrrolidinyl)-pyrido[2,3-d]pyrimidine group, cannot be an aromatic ring, because of the mandatory presence of the C=Y group (wherein Y is O or S) in the ring and the substituent group $R^1$, which does not include hydrogen, on the nitrogen atom of the ring. *See Beasley*, page 4. Such a ring structure makes it impossible for a conjugated cyclic

system of six pi electrons to exist. Therefore, the compounds of *Beasley* do not contain the group corresponding to group $R^5$ of the compounds of the present invention. Thus, *Beasley* does not anticipate the presently claimed invention.

Accordingly, Applicants respectfully request this rejection be withdrawn.

**B. Horn et al.**

The Office has also maintained the rejection of claims 6-9, 11-15, and 17 under 35 U.S.C. § 102(b) as being anticipated by Horn et al. (EP 0420064) ("*Horn*"). Office Action, pages 3 and 4. Specifically, the Office contends that *Horn* teaches that its compounds could be used for "sexual dysfunction (see page 5, line 18)," including "erectile dysfunction" recited in the presently claimed invention. *Id.* at page 3. Therefore, the Office concludes that "the instant claims do not recite 'new use' of the compounds. The mode of action of NO-synthase is a property inherently possessed by the compounds of the reference." *Id.* at pages 3-4. In support of its argument, the Office further cites *In re May*, 574 F.2d 1082, 1090, 197 USPQ 601,607 (CCPA) and relies on a statement therein that "applicants merely found a new property of the compound and such a discovery did not constitute a new use." *Id.* at page 4. Applicants respectfully disagree for at least following reasons.

1. Claims 6-9 and 11

First, claims 6-9 and 11, which recite a method of stimulating the expression of endothelial NO-synthase in a mammal, are method claims and recite a "new use" of the compounds, because *Horn* nowhere teaches that its compound could stimulate the

expression of endothelial NO-synthase. The Office's contentions that "[t]he therapeutic effect of claims 6-9 is evident from the dependent claims 12-15" and "the instantly claimed mechanism of stimulating the expression of endothelial NO-synthase is inherently taught in the reference" set forth on pages 4-5 of Office Action dated March 20, 2003, as well as on pages 3-4 of the outstanding Office Action, adopt an improper hindsight approach. Without the disclosure of the present application, the Office has failed to provide any evidence that stimulating the expression of endothelial NO-synthase in a mammal could necessarily lead to the therapeutic effect on the diseases recited in, for example, claim 12. Further, the Office has failed to provide any basis in fact and/or technical reasoning, outside of the disclosure of the present invention, to support its rejection based on inherent anticipation.

In addition, the Office has improperly relied on *In re May*, 574 F.2d 1082, 1090, 197 USPQ 601,607 (CCPA). In *May*, the prior art reference teaches "a method for effecting analgesia." 197 USPQ 601, 607. Claim 1 of the application in *May* recites "a method for effecting nonaddictive analgesia." *Id.* The court decided that "nonaddictiveness" is a property of the compounds disclosed in the prior art reference; therefore, discovery of such a property does not constitute a new use. *Id.*

In this case, however, *Horn* does not teach that its compounds could be used to stimulate the expression of endothelial NO-synthase in a mammal. Therefore, stimulating the expression of endothelial NO-synthase in a mammal is a new use of the compounds of the present invention. Accordingly, unlike the prior art reference in *May*, *Horn* does not anticipate a "method of stimulating the expression of endothelial NO-synthase in a mammal" as recited in, for example, claim 6 of the present invention.

2. Claims 12-15 and 17

Second, in a proper § 102(b) rejection, the prior art reference must teach each and very element of the present claims. M.P.E.P. § 2131. Claims 12-15 and 17 recite a "method of treating a mammal suffering from a disease chosen from . . . wherein the physiologically active amount of the compound according to the general formula (I) . . . stimulates the expression of endothelial NO-synthase in the mammal." *E.g.*, claim 12 (emphasis added). However, the Office has failed to provide any evidence that *Horn* teaches that its compounds stimulate "the expression of endothelial NO-synthase in the mammal." In addition, the Office has failed to provide any basis in fact and/or technical reasoning, outside of the disclosure of the present invention, to support its rejection based on inherent anticipation.

Furthermore, the holding of *May* does not apply here, because in *May* there is no issue of missing element.

Therefore, Applicants respectfully request this rejection be withdrawn.

**C. Yamada et al.**

Finally, the Office has rejected claims 6-17 under § 102(b) as being anticipated by Yamada et al. (WO 00/51970) ("*Yamada*"). Office Action, pages 4-5. Specifically, the Office contends that *Yamada* teaches "amide compounds (see formula (I) in page 2 and the species of Example 8)," which "have therapeutic effect on various diseases, including stroke, etc. (see page 1, lines 18+)." Therefore, the Office concludes that *Yamada* anticipates claims 6-17. Applicants respectfully disagree for at least following reason.

Claims 6-17 are method claims reciting stimulation of the expression of endothelial NO-synthase in a mammal. *Yamada* nowhere teaches that its compound could stimulate the expression of endothelial NO-synthase. Instead, *Yamada* clearly teaches that its compounds potentiate the cholinergic activity and therefore are useful for treating various disorders of the central nervous system, such as stroke. Page 1, line 18 - page 2, line 2. Therefore, as indicated by *Yamada*, even for treating the same disease, a compound can assert the effect through various and different mechanisms. (Applicants respectfully request the Office also consider this teaching by *Yamada* in the rejection of claims 6-9, 11-15, and 17 under 35 U.S.C. § 102(b) as being anticipated by *Horn* in section B.) Here, stimulating the expression of endothelial NO-synthase is a "new use" of the compounds of the present invention, as *Yamada* nowhere teaches the stimulation of the expression of endothelial NO-synthase.

In addition, as discussed above, the Office's contention that "[t]he therapeutic effect of claims 6-10 is evident from the dependent claims 12-16" apparently adopts a hindsight approach, because, without the disclosure of the present invention, the Office has failed to provide any evidence that stimulating the expression of endothelial NO-synthase in a mammal could necessarily lead to the therapeutic effect on the diseases recited in, for example, claim 12. Further, the Office has failed to provide any basis in fact and/or technical reasoning, outside of the disclosure of the present invention, to support its rejection based on inherent anticipation.

Therefore, this rejection is improper. Accordingly, Applicants respectfully request this rejection be withdrawn.

## III. Allowable Subject Matt r

The Office has indicated that claims 5 and 21-23 "are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims." Office Action, page 5.

Applicants respectfully submit that claim 5 is currently in an independent form, therefore, should be allowed.

In addition, as discussed above, Applicants reasonably believe that rejections of claim 12, on which claims 21-23 are dependent, should be withdrawn. Thus, Applicants respectfully reserve the right to rewrite claims 21-23 in independent form if the Office maintains its rejections of claim 12.

## IV. Conclusion

In view of the foregoing remarks, Applicants respectfully request reconsideration and reexamination of this application, and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our Deposit Account No. 06-0916.

Respectfully submitted,

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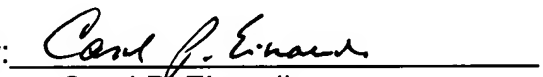
By: 
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